

CDRH/ODE/DSD Regulation of Hemostatic Devices

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Hemostatic Workshop

Presentation Outline

- FDA/CDRH Basics
- Device Classification
- Hemostatic Devices Regulated by the Division of Surgical Devices (DSD)
- *De Novo*
- Reference Materials

Important Dates Regarding the Food and Drug Administration

- 1862 - President Lincoln appoints Charles M. Wetherill to serve in the new Dept. of Agriculture. The Bureau of Chemistry begins.
- 1879 - Peter Collier, chief chemist, USDA begins investigating food adulteration. The next year he recommends a national food and drug law.
- 1906 - The Food and Drugs Act prohibits interstate commerce of misbranded or adulterated foods, drinks and drugs.

Important Dates Food and Drug Administration

- 1938 - Food, Drug and Cosmetic Act prohibited marketing of adulterated or misbranded medical products.
 - FD&C Act required new drugs to be shown as safe before marketing.
- 1962 – Kefauver-Harris Drug amendments require demonstration of drug efficacy before marketing.
- 1976 – Medical Device Amendments requires the safety and effectiveness of medical devices.

Important Dates Center for Devices and Radiological Health

- 1969 - Literature review by HEW verifies 10,000 injuries associated with medical devices over 10-year period.
- 1970 - The Cooper Committee issues a final report recommending inventory and classification of medical devices as a first step in legislating the safety and effectiveness of medical devices.
- 1971 - All FDA medical device activities are transferred from the Bureau of Drugs to the Office of Assistant Commissioner for Medical Affairs.
- 1974 - The Bureau of Medical Devices and Diagnostic Products is established.
- 1976 Medical Device Amendments

Medical Device Amendments

- 1976 - The Medical Device Amendments to the FD&C Act are enacted and provide the authority to ensure safe and effective devices through classification, premarket notification, premarket approval and postmarket controls.
- Section 201.[321](h)(1) of the Food, Drug and Cosmetic Act (i.e., The Medical Device Amendments), defines a device as:
 - "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent or other similar or related article, including any component, part or accessory, which is -

Medical Device Amendments (Continued)

- (2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- (3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes."

Device Classification

- Approximately 1700 general categories of classified medical devices are included in 16 classification regulations found in 21 CFR Part 800-1299 by the Classification Panels.
- Class I -- General Controls
- Class II -- General Controls + Special Controls
- Class III -- Premarket Approval
- Unclassified Devices

Unclassified Devices

- Devices which existed before the device amendments to the FD&C Act (1976) but were not classified by the classification panels which met in the late 1970s/early 1980s and endeavored to classify all known devices.
- Also referred to as Pre-Amendment devices.

Principal Unclassified Hemostatic Devices Regulated by DSD

- Wound Dressings for external wounds made with chitosan
- Combination product wound dressings for external wounds that include thrombin
- Wound dressings for external wounds that include oxidized cellulose or collagen
- Wound dressings for external wounds that include zeolite or various clays (bentonite or kaolin are principal examples)

Class I General Controls

- Prohibit adulterated or misbranded devices.
- Grant FDA authority to ban certain devices and to restrict sale, distribution or use of devices.
- Provide for notification of risks and of repair, replacement or refund.
- Govern Good Manufacturing Practices, records, reports, and inspection.
- Require domestic device manufacturers, initial distributors (importers) and distributors to register establishments and for manufacturers to list devices.

Principal Class I Hemostatic Devices Regulated by DSD

- (21 CFR §) 878.4014 – Nonresorbable gauze/sponge for external use
- 878.4018 Hydrophilic wound dressing
- 878.4450 Nonabsorbable internal gauze
- 878.4800 Manual Surgical Instrument
- 878.5900 Non-pneumatic tourniquet
- 880.5240 Medical adhesive tape and bandage

Class II – Special Controls

- General controls as in Class I.
- Sufficient information exists to establish special controls (written into the regulation or a guidance document).
- May include mandatory performance standards, patient registries, post-market surveillance, etc.

Class II – Special Controls (Cont.)

- Used to determine Substantial Equivalence via a Premarket Notification Application based on Section 510(k) of the FD&C Act (21 CFR 807)
- If Clinical Study Data are needed
Investigational Device Exemption (IDE)
21 CFR 812

Substantial Equivalence

- This terminology means that the new device has similar indications for use or intended use and the same technological characteristics as the predicate device
- If different (but related) technology does not raise different questions regarding safety and effectiveness than the predicate [from 21 CFR §807.100(b)].

Factors used to Establish Substantial Equivalence

- Intended Use/Indications
- Device Description
- Specification of Device Materials
- Manufacture and Sterilization
- Description of the Packaging
- Product Characterization (biocompatibility, device characteristics, product specifications, expiration dating, animal studies, clinical studies)
- Labeling

Principal Class II Hemostatic Devices Regulated by DSD

- (21 CFR §) 878.4400 – Electrosurgical cutting and coagulation device and accessories
- 878.4452 – Non-absorbable, expandable, hemostatic sponge for temporary internal use – XSTAT
- Most current unclassified wound dressings for external use proposed for Class II regulation

Class III – Premarket Approval (PMA)

- General controls as in Class I.
- Information is insufficient to assure that general controls and special controls provide reasonable assurance of safety and effectiveness.
- Generally, such devices are represented to be life-sustaining or life-supporting, are implanted in the body, or present an unreasonable potential risk of illness or injury.

Principal Class III Hemostatic Devices Regulated by DSD

- (21 CFR §) 878.4490 – Absorbable hemostatic agent and dressing
- No regulation number – Tissue Sealants when they have general/plastic surgery indications

Evaluation of Automatic Class III Designation: *De Novo* Provisions

- Devices that FDA has not previously classified are “automatically” or “statutorily” classified into class III based on section 513(f)(1) of the FD&C Act.
- Food and Drug Administration Modernization Act of 1997 (FDAMA) said that once a device was determined to be NSE, a manufacturer could, according to section 513(f)(2), submit a *de novo* application to FDA for lower risk devices when they were “automatically” classified into Class III by operation of section 513(f)(1).

Evaluation of Automatic Class III Designation: *De Novo* Provisions

- The provisions of 513(f)(2) were modified as part of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), which removed the requirement that a device be reviewed first under a 510(k) and found NSE prior to submission of a *de novo*. If a submitter cannot identify a legally marketed Class I or Class II predicate device, but believes that their device is appropriate for classification into Class I or Class II, they may submit a *de novo* without a preceding 510(k) and NSE (“direct *de novo*”).

Evaluation of Automatic Class III Designation: *De Novo* Provisions

- De Novo Classification Process (Evaluation of Automatic Class III Designation); Draft Guidance for Industry and Food and Drug Administration Staff – released for comment on August 14, 2014.
- <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm273903.pdf>

De Novo Summaries

- Link to summaries of all previously granted *de novo* applications located here:
- <http://www.fda.gov/aboutfda/centersoffices/officeofmedicalproductsandtobacco/cdrh/cdrhtransparency/ucm232269.htm>
- XSTAT classification order and decision summary, respectively are located here:
 - http://www.accessdata.fda.gov/cdrh_docs/pdf13/K130218.pdf
 - http://www.accessdata.fda.gov/cdrh_docs/reviews/K130218.pdf

Early Contact with CDRH; the Qsub Process

- QSub – set up a meeting with review Branch and get feedback regarding all aspects of regulatory process for a device.
- <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm311176.pdf>

Early Contact with CDRH; the IDE for Early Feasibility Studies

- Early Feasibility Study (EFS) – EFS studies allow for early clinical evaluation of devices to provide proof of principle and initial clinical safety data. These studies may be appropriate early in device development when clinical experience is necessary because nonclinical testing methods are not available or adequate to provide the information needed to advance the developmental process.
- <http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm279103.pdf>
- DSD Contacts for EFS
 - Betsy Ballard, betsy.ballard@fda.hhs.gov, 301.796.6970
 - Long Chen, long.chen@fda.hhs.gov, 301.796.6970

Additional Reference

- Device Advice Website:
- <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/default.htm>

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